Practitioner's Docket No. MPI00-252P1RM

REMARKS

Claims 1-31 have been canceled, without prejudice, and new claims 32-61 have been added. Accordingly, claims 32-61 will be pending upon entry of the instant amendment. No new matter is added by virtue of the amendments. Support for new claims 32-61 can be found throughout the specification and claims as originally filed. For example, support may be found at page 34, beginning on line 20, at page 37, beginning on line 6, at page 41, beginning on line 26, and at page 62, beginning on line 11.

Objections to the Specification

The disclosure was objected to because it contains blank underlined spaces.

Applicants have amended the specification to remove all blank underlined spaces and additionally to remove hyperlinks. Applicants respectfully request reconsideration and withdrawal of the Examiner's objections to the specification.

The Rejection of Claims 1-7 and 12 under 35 U.S.C. §101 Should Be Withdrawn

Claims 1-7 and 12 were rejected under 35 U.S.C. 101 because "the claimed invention is not supported by either a substantial asserted utility or a well established utility." Applicants respectfully traverse this rejection.

The Examiner assumes the asserted utility of the polypeptide and nucleic acid molecule is solely "determining pharmacological properties" and subsequently asserts the claimed invention is not supported by a substantial asserted utility or well-established utility. Applicants respectfully point out that a substantial and well-established utility, which would have been credible to one skilled in the art at the time of invention, is clearly disclosed in the instant specification. The specification discloses the differential expression of the 52906 gene in congestive heart failure (CHF) heart tissue versus normal heart tissue (see for example, Table 3). 52906 is expressed in CHF tissue but is not expressed in normal heart. Thus, a person of skill in the art would appreciate the usefulness of the 52906 molecule as a diagnostic tool for the identification of diseased CHF tissue, and/or the use of 52906 molecules for the identification of potential therapeutics for CHF. (See, e.g., pages 68-69)

As acknowledged by the Examiner, the instant application has provided a description of isolated 52906 nucleic acid sequences of SEQ ID NO:1 and 3 encoding an amino acid sequence of SEQ ID NO:2. In addition, the specification sets forth use of the described 52906 compositions in methods for diagnostics for disorders, including, for example, cardiac-related disorders (see for example, page 68-69). Applicants submit the utility of diagnostics is an accepted substantial and real world utility in the pharmaceutical industry. Utility of diagnostics is well established and evident by the numerous issued patents relating to subject matter comprising

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diagnostic applications. Still further, the Office recognizes that intermediate, or research tool utilities can and do satisfy the Utility requirement. For example MPEP 2107.01 section addressing research tools:

> *Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds).*

Still further, Applicants believe situations akin to the Applicant's present position have been acceptable to the Office as meeting the utility requirements For example, Applicants respectfully direct the Examiner to Example 5 of the *Revised Interim Written Description Guidelines Training Materials*, wherein the *Guidelines* provide a claim directed to an "isolated protein consisting of the amino acid sequence set forth in SEQ ID NO:1" with an accompanying specification that discloses that "when the protein is contacted with whole blood, the protein will specifically bind with another protein X such that X can be isolated and quantified." The *Guidelines* set forth this Example as a specific instance wherein the claims are exemplary as a well-established utility under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph "if the art disclosed at the time of filing that, e.g., an increased level of X correlates with an increased risk of heart disease" (page 35).

Similarly, in Example 12 of the *Revised Interim Written Description Guidelines Training Materials*, wherein the *Guidelines* provide a claims directed to an isolated receptor, receptor A, methods to identify materials which bind to the receptor and a monoclonal antibody which specifically binds to the receptor. The accompanying specification discloses an asserted, specific utility for identifying candidate therapeutics by identifying compounds that bind the receptor The *Guidelines* set forth this Example as a another instance wherein the claims are exemplary as a well-established utility under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph if the specification "discloses that receptor A is present on the cell membranes of melanoma cells but not on the cell membranes of normal skin cells" and prior art discloses "that it is desirable to selectively detect melanoma cells as opposed to normal skin cells so to diagnose hat type of cancer" (pages 69-70).

In the present application, the specification discloses the differential expression of the 52906 gene in CHF heart tissue versus normal heart tissue. Additionally, there are also numerous articles published before the filing date of the instant application that indicate that it is necessary to selectively detect CHF tissue as opposed to normal heart tissue to diagnose heart failure and find therapeutics for the disease. Still further, contrary to the Examples in the Guidelines, Applicants have in fact asserted such uses in the

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present application. Thus, Applicants respectfully submit that a well-established utility, which would have been credible to one skilled in the art at the time of invention, is clearly disclosed in the instant specification. As such, it is believed Applicants have in fact met the requisite burden in order to establish the requirements for a well-established utility.

Applicants respectfully submit the utility rejection set forth in the present instance is therefore improper and a rebuttal of the asserted utility has not been effectively made in the present case. The steps that should be taken in order to make a rejection should fall under MPEP 2107 (II)(C), where the Examiner is required to make a proper *prima facie* showing of no specific and substantial credible utility. See MPEP 2107(II)(C) (emphasis added):

> *(I) Where the asserted utility is not specific or substantial, a prima facie showing* ***must establish that it is more likely than not*** *that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie* ***showing must contain the following elements****:*
> *(i) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established;*
> *(ii)* ***Support for factual findings*** *relied upon in reaching this conclusion; and*
> *(iii) An evaluation of* ***all relevant evidence of record****, including utilities taught in the closest prior art.*

The Examiner has not made a sufficient showing to establish more likely than not the utility set forth in the present specification would not be substantial or well established, as sufficient support or factual findings have not been relied upon to make such a showing to rebut Applicants' assertion that the use of the claimed compositions in diagnostics assays an/or identification of potential therapeutics would more likely than not be useful.

Applicants therefore respectfully request the Examiner's rejection under 35 U.S.C. §101 be reconsidered and withdrawn.

The Rejection of Claims 1-7 and 12 under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1-7 and 12 were also rejected under 35 U.S.C. 112, first paragraph, because the claimed invention purportedly is not supported by a substantial utility or well established utility, thus one skilled in the art would not know how to use the claimed invention. The rejection is traversed.

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As discussed above, the 52906 molecules of the present invention are in fact supported by a substantial and well-established utility that would have been readily apparent to one of skill in the art. For the reasons discussed above, Applicants thus respectfully reconsideration and withdrawal of the Examiner's rejection under 35 U.S.C. §112.

The Rejection of Claims 1, 3-7 and 12 under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1, 3-7 and 12 were rejected under 35 U.S.C. 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner states that the "essential feature of the invention is the nucleic acid molecule which encodes a potassium channel subunit of SEQ ID NO:2, and one skilled in the art cannot envision the full genus of molecules of the claimed variant nucleic acid molecules."

Applicants respectfully traverse this rejection, however, in the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, the Applicants have canceled claims 1-7 and 12 and have added new claims 32-61.

The limitations within these new claims are fully enabled within the specification as Applicants have provided teachings for every element needed for one of skill in the art to practice the claimed invention. Firstly, Applicants have taught a domain within the 52906 polypeptide which is conserved and essential for activity of the polypeptide, namely the ion transport protein domain located at about residues 472 to 661 of SEQ ID NO:2 (see for example, Figure 2). Secondly, by having identified the region necessary for activity, Applicants have taught which coding regions of the nucleotide sequence are amenable to alterations as well as those which are not amenable to alterations. The specification teaches one how to generate functional variants of 95% identity by performing nucleotide substitutions leading to amino acid substitutions used in the claimed invention. As defined on page 31, "An 'essential' amino acid residue is a residue that, when altered from the wild-type sequence of 52906..., results in abolishing a 52906... activity such that less than 20% of the wild-type activity is present. For example, conserved amino acid residues in 52906... are predicted to be particularly unamenable to alteration... A 'conservative amino acid substitution' is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain." The Applicants have also defined which of the amino acids have similar side chains, thereby providing a skilled artisan the necessary tools to generate functional variants of the polypeptide used in the claimed invention.

Finally, Applicants have provided teachings for one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired potassium channel activity. As taught on page 26-28 of the specification, such biological activity can include (1) interacting with a non-52906...

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protein molecule; (2) activating a 52906...-dependent signal transduction pathway; (3) modulating the release of neurotransmitters; (4) modulating membrane excitability; (5) influencing the resting potential of membranes, wave forms and frequencies of action potentials, and thresholds of excitation; (6) binding a cyclic nucleotide; (7) contributing to the formation of potassium channels; (8) contributing to the formation of calcium-activated, voltage independent potassium channels; (9) modulating repolarization of the neuronal cell membrane; (10) contributing to the formation of voltage-gated potassium channels; (11) contributing to the formation of cyclic nucleotide-gated potassium channels; (12) modulating the flow of K^+ ions through a cell membrane; and (13) modulating processes which underlie learning and memory, such as integration of sub-threshold synaptic responses and the conductance of back-propagating action potentials... modulation of resting potential of membranes, wave forms and frequencies of action potentials, and thresholds of excitation; participation in signal transduction pathways, and modulation of processes such as integration of sub-threshold synaptic responses and the conductance of back-propagating action potentials in, for example, neuronal cells or muscle cells." Based on these activities, one can perform assays on specific sequences to determine whether or not such sequences have the desired biological activities. Such assays include, for example, assays which measure the flow of K^+ ions through a cell membrane and/or by measuring the transmission of signals in an electrically excitable cell, e.g., a neuronal cell or a muscle cell. (see for example, page 70, lines 14-20). Performing such assays to determine whether or not a sequence 95% identical to SEQ ID NO:1 or 3 or a polypeptide 95% identical to SEQ ID NO:2 has the desired properties would not constitute undue experimentation. Therefore, Applicants have provided all of the necessary information to enable one of skill in the art to 1) identify regions within the polypeptide of the claimed invention which may be altered while maintaining activity; 2) generate active variants; and 3) perform assays to determine whether or not the sequences generated do in fact have the desired potassium channel activity.

Therefore, contrary to the Examiner's assertions, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of new claims 32-61. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, First Paragraph, rejection.

The Rejection of Claims 1, 3-7 and 12 under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 1, 3-7 and 12 were rejected under 35 U.S.C. 112, second paragraph, as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that claim 1 recites the term "hybridizes under stringent conditions" or "hybridizes" and asserts the term is "ambiguous because it is a relative term and it [sic] not clear what is the metes and bounds of the claimed nucleotide."

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Applicants respectfully traverse this rejection. Applicants submit that the term "hybridizes under stringent conditions" as used in the claims would be well understood in view of the knowledge of one of skill in the art, combined with the teachings of the specification. However, in the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, Applicants have canceled claims 1-31 in favor of new claims 32-61. It is believed the presentation of new claims 32-61 renders the present rejection moot. Applicants thus respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, Second Paragraph, rejection.

The Rejection of Claims 1, 3-7 and 12 under 35 U.S.C. § 102 Should Be Withdrawn

Claims 1, 3-7 and 12 were rejected under 35 U.S.C. 102(b) as being anticipated by Adelman (WO 98/11139). The Examiner states that Adelman discloses "nucleic acid encoding a potassium channel which is 99.8% best local similarity to the claimed nucleic acid encoding SEQ ID NO:2. Adelman et al discloses vectors and host cells and method of making recombinant protein using the host cell."

The rejection is traversed. Applicants submit the threshold of homology is intended to include homology over the entire length of the molecule. In the interest of clarification, however, new claims 32-61 have addressed the Examiner's concerns. Applicants submit new claim 32 recites "a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence at least 95% identical to the entire length of the amino acid sequence of SEQ ID NO:2, wherein the polypeptide has potassium channel activity," rendering the rejection moot. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102(b) rejection.

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CONCLUSIONS

In view of the amendments and remarks herein, Applicants respectfully submit that the objections and rejections presented by the Examiner are now overcome and that this application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is believed that this paper is being filed timely and no extensions of time are required. In the event any extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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